



DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

FOR US POSTAL SERVICE DELIVERY:

Office of Laboratory Animal Welfare
6700B Rockledge Drive, Suite 2500, MSC 6910
Bethesda, Maryland 20892-6910
Home Page: <http://grants.nih.gov/grants/olaw/olaw.htm>

FOR EXPRESS MAIL:

Office of Laboratory Animal Welfare
6700B Rockledge Drive, Suite 2500
Bethesda, Maryland 20817
Telephone: (301) 496-7163
Facsimile: (301) 402-7065

December 9, 2019

Re: Animal Welfare Assurance
#A3284-01 (OLAW Case 1Y)

Dr. Jill C. Pipher
Vice President for Research
Brown University
47 George St. - Box 1937
Providence, Rhode Island 02912

Dear Dr. Pipher,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your December 5, 2019 letter providing clarification on the incident reported on September 20, 2019 at your institution.

Thank you very much for promptly providing additional information to clarify your programmatic corrections. From this clarification, our office understands that your institution has a robust method for tracking animals, tracking funding sources and preventing recurrence of the noncompliances described in your initial report. We thank you for ensuring that no charges for unauthorized activities were made to NIH grants. OLAW concurs with the actions taken by your institution to comply with the PHS Policy on Humane Care and Use of Laboratory Animals. We appreciate having been informed of this matter and find no cause for further action by this office.

Sincerely,

(b) (6)

Nicolette Petervary, VMD, DACAW
Animal Welfare Policy Specialist
Office of Laboratory Animal Welfare

CC: IACUC contact



BROWN

Jill C. Pipher
Office of the Vice President for Research
Elisha Benjamin Andrews Professor of
Mathematics

December 5, 2019

Nicolette Petervary, VMD, DACAW
Animal Welfare Policy Specialist
Office of Laboratory Animal Welfare
(OLAW)
National Institutes of Health
Rockledge 1, Suite 360
6705 Rockledge Drive
Bethesda, MD 20892

RE: Noncompliance Report, Assurance A3284-01 (OLAW Case 1Y)

Dear Dr. Petervary:

Thank you for your letter dated October 15, 2019 in response to the Brown University ("Brown") report of September 20, 2019, in which I provided you with the results of a review conducted by the Brown Institutional Animal Care and Use Committee. I also appreciate the time you took to speak with members of Brown's Office of Research Integrity via phone to clarify the requests for additional information.

As discussed on these phone calls, in conducting this thoughtful and thorough review, the IACUC subcommittee interviewed many past and present members of a large laboratory. Importantly, these witness interviews confirmed that there is a very high level of commitment by the majority of laboratory members to compliance, research integrity, and animal welfare. The IACUC subcommittee did not note any systemic concerns; rather, as indicated in the prior report, two specific laboratory members were identified as responsible for the reported noncompliance.

Also as discussed via phone, this laboratory maintains a single IACUC-approved protocol with several sub-studies funded by multiple funding sources. The IACUC confirmed that there was active National Institutes of Health (NIH) funding supporting animal work in the laboratory during the time-frame identified for the reported noncompliance incidents, but did not seek to conduct a one-to-one analysis of the funding source for each identified incident.

The IACUC can further confirm that Brown's Center for Animal Resources and Education (CARE) maintains an internal process and accounting mechanism to ensure that charges associated with animal activities are allocated to the appropriate NIH awards. The NIH awards associated with this IACUC protocol for the time-period subject to this review were as follows: National Heart, Lung, and Blood Institute (NHLBI) award #5P01HL114501-05; NHLBI award #5R01HL115813-04; NHLBI award #GR104568; and NHLBI award #M15A12057.

Please find responses to the questions enumerated in your October 15th letter below:



BROWN

Jill C. Pipher
Office of the Vice President for Research
Elisha Benjamin Andrews Professor of
Mathematics

1) Approximate dates of occurrence: The IACUC subcommittee reviewed concerns shared by witnesses dating from calendar year 2013 through July 2019. The IACUC did not conduct its review in such a way that it attempted to identify precise dates of reported incidents, as it sought to protect the confidentiality of witnesses. Requests for and recording of precise dates could have identified certain current and past members of the laboratory; as such, the IACUC subcommittee sought to accurately identify approximate time-frames.

2) Species affected: Mice

3) Approximate number of animals affected: While the IACUC subcommittee's review did not seek to identify with precision the total number of mice impacted, based on the information provided by witnesses, the subcommittee estimates the total number of mice affected by noncompliance to be no more than 300 in total.

4) Confirmation that no charges for unauthorized activities are made to the grants as per NOT-OD-07-044: Following a careful review of the requirements set forth for in the *NIH Policy on Allowable Costs for Grant Activities When Terms and Conditions are not Upheld*, Brown has confirmed that no charges for unauthorized activities were made to NIH grants.

Brown University is committed to protecting the welfare of animals used in research and appreciates the guidance and assistance provided by OLAW in this regard. If you have any questions or concerns regarding this report, please contact (b) (6) at (b) (6) or (b) (6)

Sincerely,

(b) (6)

Jill C. Pipher, PhD
Vice President for Research, Institutional Official
Brown University

cc: Diane Hoffman-Kim, PhD, IACUC Chair
Lara Helwig, DVM, Attending Veterinarian

(b) (6)



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October 15, 2019

Re: Animal Welfare Assurance
#A3284-01 (OLAW Case 1Y)

Dr. Jill C. Pipher
Vice President for Research
Brown University
47 George St. - Box 1937
Providence, Rhode Island 02912

Dear Dr. Pipher,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your September 26, 2019 letter. The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your letter sent September 20, 2019 regarding noncompliance with the Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals at your institution. This letter had not been preceded by a preliminary report to OLAW.

According to the information provided, our office understands that upon investigation of an animal welfare complaint, the Institutional Animal Care and Use Committee (IACUC) found that laboratory members utilizing a species of rodent performed euthanasia techniques inconsistent with the IACUC approved protocol, IACUC policies, and the AVMA Guidelines for the Euthanasia of Animals. In addition, genotyping and identification methods deviated from the approved protocol and IACUC policy, and colony management resulted in overcrowding and violation of IACUC policy.

Corrective measures included suspension of animal use privileges for 30 days, retraining by care staff, and requiring the lab members to perform procedures under observation by a veterinarian before animal use privileges would be reinstated. The Principal Investigator (PI), was required to develop and submit a plan to the IACUC that ensured that the IACUC approved protocol was readily available to lab members. The PI also was requested to consider hiring a colony manager, and to ensure that onboarding of new lab members included training in compliance and utilization of the PI and Animal Care for questions regarding animal work.

Based on its assessment of this explanation, OLAW understands that measures have been taken to prevent recurrence of this problem. OLAW concurs with the actions taken by your institution to comply with the PHS Policy on Humane Care and Use of Laboratory Animals. However, while tracking animals in a laboratory with a breeding operation can be challenging, please be aware that the inability to determine which grants were affected by these noncompliances may suggest animal inventory, animal tracking, or protocol congruence issues that might be programmatic in nature.

We also request some additional information. Please provide the following to this office no later than **December 7, 2019** by emailing olawdco@mail.nih.gov and carbon copying nicollette.petervary@nih.gov:

1. Approximate dates of occurrence
2. Species affected
3. Approximate number of animals affected
4. Confirmation that no charges for unauthorized animal activities are made to the grants as per NOT-OD-07-044.

Page 2 – Dr. Pipher
October 15, 2019
OLAW Case A3284-1Y

We appreciate being informed of these matters and look forward to your response.

Sincerely,

 (b) (6)

for Nicolette Petervary, VMD, DACAW
Animal Welfare Policy Specialist
Office of Laboratory Animal Welfare

CC: IACUC contact



BROWN

A3284-1Y

September 20, 2019

Brent Morse, DVM
Director, Division of Compliance
Oversight
Office of Laboratory Animal
Welfare (OLAW)
National Institutes of Health
Rockledge 1, Suite 360
6705 Rockledge Drive
Bethesda, MD 20892

RE: Noncompliance Report, Assurance D16-00183 (A3284-01)

Dear Dr. Morse:

The Brown University Institutional Animal Care and Use Committee (IACUC), through the Institutional Official (Jill Pipher, PhD), is writing to provide OLAW with a report of a review conducted by the IACUC.¹ The IACUC received a concern from an anonymous party pertaining to rodent euthanasia procedures conducted under a single IACUC protocol specific to two members of a laboratory. The IACUC found that other concerns raised by witnesses during the course of the review were also within its charge to evaluate.

The IACUC discussed the results of its review and made its final determination at its convened meeting in September 2019. The IACUC considered both the original concern and the other concerns raised in reaching its conclusion and establishing a corrective action plan.

The IACUC concluded that the following noncompliant actions were taken by one or both of the individuals cited in the concern:

- 1) Performance of euthanasia methods inconsistent with Brown University IACUC Policy, American Veterinary Medical Association (AVMA) guidelines, and the IACUC-approved protocol;
- 2) Performance of rodent genotyping and rodent identification methods inconsistent with IACUC Policy and the IACUC-approved protocol; and
- 3) Colony management issues in violation of IACUC Policy, which, in part, resulted in cage overcrowding.

¹ The concerns reported took place during the period when National Institutes of Health (NIH) funding was awarded to the laboratory under several different grants. The IACUC review did not reveal which NIH funding aligned with each noncompliance incident.

In addition, and in response to concerns raised through the IACUC's review, the IACUC concluded that certain laboratory members did not have appropriate access to and/or knowledge of procedures in the IACUC-approved protocol.

The IACUC issued the following corrective action plan:

- 1) Suspension of the two laboratory members for a period of 30 calendar days from conducting any activities involving the use of animals, with reinstitution of privileges subject to retraining by Animal Care and observation of these individuals performing the procedures at issue to the satisfaction of a veterinarian;
- 2) Required modification of the IACUC-approved protocol to add a euthanasia procedure the laboratory intends to use, followed by observation by Animal Care of lab members who will be performing this method of euthanasia;
- 3) Prompt submission by a Principal Investigator (PI) of the IACUC protocol of a plan to ensure that the IACUC-approved protocol is always available in the laboratory to all laboratory members²;
- 4) Consideration by the PIs of the IACUC-approved protocol of instituting a laboratory manager or colony manager position to prevent recurrence of some of the concerns identified³; and
- 5) Implementation of an individual meeting with a PI of the IACUC protocol for onboarding new personnel, in which the importance of complying with the IACUC-approved protocol is reiterated and the PI emphasizes his/her/their role as a resource if any animal welfare concerns or questions arise, and the availability of Animal Care as a resource for all animal researchers in the laboratory.

Brown University is committed to protecting the welfare of animals used in research and appreciates the guidance and assistance provided by OLAW in this regard. If you have any questions or concerns regarding this report, please contact (b) (6)

(b) (6) at (b) (6) or (b) (6)

Sincerely,

(b) (6)

Jill C. Pipher, PhD
Vice President for Research, Institutional Official
Brown University

cc: Diane Hoffman-Kim, PhD, IACUC Chair
Lara Helwig, DVM, Attending Veterinarian

² In addition, the IACUC requires that all current and future laboratory members sign an attestation affirming that they have read and understand the IACUC-approved protocol.

³ Importantly, the laboratory has already opted to contract with Animal Care for colony management services for some of its mouse colonies.

(b) (6)

Na, Jane (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Friday, September 20, 2019 2:42 PM
To: (b) (6)
Cc: Jill Pipher; Diane Hoffman-Kim; Lara Helwig; (b) (6) OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Noncompliance report: Assurance D16-00183 (A3284-01)

Thank you for this report. We will send an official response soon.

Jane

Jane Na, DVM, CPIA
Veterinary Medical Officer
Office of Laboratory Animal Welfare
National Institutes of Health
Phone (301) 402-1922
E-fax (301) 451-5609

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From: (b) (6)
Sent: Friday, September 20, 2019 2:31 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Jill Pipher <jill_pipher@brown.edu>; Diane Hoffman-Kim <diane_hoffman-kim@brown.edu>; Lara Helwig <lara_helwig@brown.edu>; (b) (6)
Subject: Noncompliance report: Assurance D16-00183 (A3284-01)

Dear Dr. Morse,

Attached please find a report of noncompliance discussed at the September 2019 convened meeting of the Brown University IACUC.

Please do not hesitate to contact me if you have any questions.

Sincerely,
(b) (6)

(b) (6)